REMARKS

The specification was amended to correct typographical errors.

Claims 1-18 were pending. Claims 1-18 have been amended to clarify the claim language. Support for the recitation of the term "nucleic acid drug" is found throughout the specification, for example at page 5, lines 22-26 and in the Examples. No new matter has been added.

Claim 1 has been amended also to incorporate the limitation of claim 2 and the relevant limitation of claim 5. Claim 3 has been amended also to incorporate the relevant limitation of claim 5. Claims 3, 4, 11 and 16 were amended to correct the claim dependency given the cancellation of claim 2.

Claim Objections

The Examiner objected to claims 12-14 and 16. Applicant has amended these claims to refer to the items in each claim in the alternative via the use of Markush group language.

Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner rejected claims 1-18 under 35 U.S.C. § 112, second paragraph, as indefinite.

Claims 1-18 were rejected as indefinite for a lack of antecedent basis for the term "the core" and for the use of phrases which, in the Examiner's view, resulted in a lack of clarity. Applicant has amended claim 1 to recite "a core" to provide antecedent basis for dependent claims, to clarify that the drug is released in the lower digestive tract, and to clarify the properties and structure of the coating. Withdrawal of the rejection of these claims is respectfully requested

in view of this amendment.

Claims 1, 15 and 18 were rejected as indefinite for a lack of clarity with respect to the location of the drug. Applicant has amended claim 1 to clarify this element, and respectfully requests withdrawal of the rejection in view of the claim amendment.

Claim 1-17 were rejected as indefinite because the metes and bounds of the term "gene-related drug" were considered unclear by the Examiner. Applicant has amended the claims to clarify the claim language with the use of the term "nucleic acid drug". Withdrawal of the rejection of these claims is respectfully requested in view of this amendment.

Claim 15 was rejected as indefinite for recitation of the terms "modified compounds thereof" and "compounds thereof". Applicant has amended claim 15 to clarify these terms, and accordingly requests that the rejection be withdrawn.

Claim 17 was rejected as indefinite because it lacks a verb. Claim 17 has been amended appropriately, and withdrawal of the rejection is respectfully requested.

Claim 18 was rejected for a lack of antecedent basis for the term "gene-related drugs". This term, in addition to being amended to recite "nucleic acid drug" (see below), has been made consistent with the term in claim 1. Applicant notes that a singular term, such as "a nucleic acid drug" as now used in the claims, has a meaning in the claims as "one or more nucleic acid drugs", and is not limited to a single drug in the claimed compositions. In view of the amendment to claim 18, Applicant respectfully requests that the rejection be withdrawn.

Rejections Under 35 U.S.C. § 112, First Paragraph

The Examiner rejected claims 1 and 18 under 35 U.S.C. § 112, first paragraph, as not enabled. Applicant has amended claim 18 to remove certain recited embodiments and respectfully requests reconsideration in view of the amendment and in view of the following

comments.

The Examiner indicated that a search of the prior indicated that certain of the recited embodiments of claim 18 were not routinely used as drugs in the lower digestive tract. Applicants have conducted a brief search of the prior art and have found at least one patent that teaches administration of triple helix forming oligonucleotides to the lower digestive tract. US Patent 5,844,110 (Gold) teaches the following at column 17, lines 51-63 about the administration of "OLIGOTRIP compounds" (triple helix forming oligonucleotides):

> The "antisense" OLIGOTRIP compounds of the present invention (also referred to hereinafter as the "active ingredients" or "active compounds"), in whatever analog prepared, are administered in a variety of dosage forms. In addition to the active ingredient, any of a number of pharmaceutically-acceptable excipients which facilitate formulation of the active ingredient into suitable dosage form can be used. In a preferred embodiment, the preparations are designed for parenteral administration. However, pharmaceutical compositions designed for oral administration in such forms as tablets, capsules, and dragees, or for rectal administration in the form of suppositories, are also considered to fall within the scope of the present invention. (Emphasis added)

Likewise, administration of phages has been described in US Patent 5,736,388 (Chada and Dubensky), which teaches the following at column 30, lines 9-21:

> Oral administration includes sublingual, buccal, and gastrointestinal delivery. Sublingual and buccal (cheek) delivery allow for rapid systemic absorption of gene transfer systems and avoid hepatic first-pass metabolism and degradation in the stomach and intestines. Unidirectional buccal delivery devices can be designed for oral mucosal absorption only. Additionally, these devices can prevent diffusion-limiting mucus buildup to allow for enhanced absorption. Delivery through the gastrointestinal tract allows for precise targeting for drug release. Depending on the formulation, bacteriophage particles can be specifically delivered to areas in the stomach, duodenum, jejunum, ileum, cecum, colon, or rectum.

Therefore, with respect to triple helix forming oligonucleotides and phages, Applicant maintain that the administration of such compounds to the lower digestive tract (by means other than the compositions of the instant claimed invention) was known in the art, and that the claims,

as amended, are fully enabled.

Accordingly, withdrawal of the rejection of claims 1 and 18 under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Rejections Under 35 U.S.C. § 102

The Examiner rejected claims 1-14 and 16 under 35 U.S.C. § 102(a) and (e) as being anticipated by US 5,654,004 (Okayama) as evidenced by US 6,180,621 (Kawamoto) and US 6,586,004 (Shimuzu). The Examiner clearly stated that the basis for this rejection was the interpretation of "gene-related drugs" as including polypeptides encoded by genes as well as compounds that affect gene expression.

Applicant has amended the claims to refer to "nucleic acid drugs" rather than "gene-related drugs." This amendment obviates the rejection based on Okayama, and Applicant respectfully requests that the rejection be withdrawn.

Rejections Under 35 U.S.C. § 103(a)

The Examiner rejected claims 1, 15 and 18 under 35 U.S.C. § 103(a) as unpatentable over US 6,096,722 (Bennett) in view of US 5,654,004 (Okayama). Applicant has amended the claims and believes the amendments obviate the rejection for the reason stated above in response to the anticipation rejection. In addition, Applicant amended claim 1 to incorporate limitations of claims 2 and 5. Given the addition of these limitations, Applicant believes that the claims are not obvious in view of the cited references.

Applicant also traverses the rejection based on the incompatibility of the combined references. The Examiner has cited Bennett for teaching administration of antisense compositions to the colon. Okayama was cited for its teaching of a particular solid preparation

coating. However, Okayama does not teaches administration of nucleic acid-based therapeutics, and therefore the two references are not properly combinable.

Moreover, even if these references are combined, Applicant asserts that there is no legally sufficient motivation to combine the references. Bennett teaches orally administered dosage forms having enteric coatings at col. 16, lines 35-37. Therefore, one of ordinary skill in the art would not be motivated to add the teachings of Okayama to the teachings of Bennett, given that (1) Bennett already teaches enteric coated delivery systems and (2) Okayama does not teach administration of nucleic acid-based therapeutics.

Further, the compositions taught by Okayama are very specific, and therefore there is no motivation for one of ordinary skill in the art to select the particular coated particles of Okayama from among all possible coated particles known in the art, given that Bennett teaches the use of other enteric coated compositions, and given that Okayama teaches administration of a different type of therapeutics.

Accordingly, withdrawal of the rejection of claims 1, 15 and 18 under 35 U.S.C. § 103(a) as unpatentable over Bennett in view of Okayama is respectfully requested.

The Examiner rejected claims 1, 15 and 18 under 35 U.S.C. § 103(a) as unpatentable over US 5,874,415 (Kufe) in view of US 5,654,004 (Okayama). Applicant has amended the claims and believes the amendments obviate the rejection as stated above.

Applicant traverses the rejection for similar reasons as those stated above in the response to the rejection of these claims based on the combination of Bennett and Okayama. Kufe teaches oral administration, but not enteric coatings. However, Kufe does teach administration to the lower gastrointestinal tract via rectal administration. Therefore, there is no reason for one of ordinary skill in the art to look to the teachings of Okayama for different compositions that would achieve the same purpose, because there is no suggestion in either of these references that it would be preferable, or even desirable, to administer the therapeutics taught by Kufe using the

specific coated compositions of Okayama. The Examiner simply has not provided the specific motivation to combine these two references as required under the law. In re Dembiczak, 50 USPQ2d 1614 (Fed. Cir. 1999).

Accordingly, withdrawal of the rejection of claims 1, 15 and 18 under 35 U.S.C. § 103(a) as unpatentable over Kufe in view of Okayama is respectfully requested.

The Examiner rejected claim 18 under 35 U.S.C. § 103(a) as unpatentable over US 6,096,722 (Bennett) in view of US 5,654,004 (Okayama) and further in view of US 6,151,525 (Soykan). The Soykan reference is included by the Examiner for its a teaching of a cosmid or a YAC.

Applicant respectfully traverses the rejection for the reasons stated above in response to the rejection based on the combination of Bennett and Okayama: the combination of Bennett and Okayama is improper and there is a lack of a legally sufficient motivation to combine these references given the respective teachings of the Bennett and Okayama references. The addition of the Soykan reference does not provide any further motivation that would be adequate to make a proper *prima facie* case of obviousness.

Accordingly, withdrawal of the rejection of claim 18 under 35 U.S.C. § 103(a) as unpatentable over Bennett in view of Okayama and further in view of Soykan is respectfully requested.

The Examiner rejected claim 18 under 35 U.S.C. § 103(a) as unpatentable over US 6,096,722 (Bennett) in view of US 5,654,004 (Okayama) and Rossi et al. (Methods 5: 1-5, 1993). The Rossi reference is included by the Examiner for its a teaching of a ribozyme. Applicant has amended the claims and believes the amendments obviate the rejection.

Applicant respectfully traverses the rejection for the reasons stated above in response to

the rejection based on the combination of Bennett and Okayama, and optionally Soykan: the combination of Bennett and Okayama is improper and there is a lack of a legally sufficient motivation to combine these references given the respective teachings of the Bennett and Okayama references. As for the Soykan reference, the addition of the Rossi reference does not provide any further motivation that would be adequate to make a proper *prima facie* case of obviousness.

In addition, Applicant disagrees with the Examiner's premise for the rejection, namely that antisense RNA and ribozymes are equivalents. Simply stated, the properties of antisense RNA and ribozymes are more different than alike, regardless of the statement made by Rossi. Ribozymes have enzymatic activity that is not found in antisense RNA molecules. Antisense RNA molecules generally are designed to hybridize fully to a given nucleic acid sequence, while ribozymes do not typically do so. Moreover, the quotation of Rossi do not indicate the molecules are equivalents. Rossi states that ribozymes can be used "in parallel or in place of" antisense RNA. That statement is not a statement of equivalence, because using one compound in parallel with another suggests that the compounds have different activities. The use of ribozymes "in place of" antisense RNA molecules also does not mean that the molecules have an equivalent effect. Therefore, the differences between antisense RNA and ribozymes compel the conclusion that these two types of molecules would not be considered "equivalent" to the person of skill in the art.

Accordingly, withdrawal of the rejection of claim 18 under 35 U.S.C. § 103(a) as unpatentable over Bennett in view of Okayama and further in view of Rossi is respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this amendment, that the application is not in condition for allowance, the Examiner is requested to call the Applicant's representative at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,
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